Protein-engineered biomaterials to generate human skeletal muscle mimics.

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Public Summary:
Skeletal muscle function, which is essential in the human body, can be lost due to injury, trauma, or diseases such as muscular dystrophy, prompting the need for in vitro models of human skeletal muscle tissue. In vitro tissue models are indispensable in performing quantitative studies of injury and disease progression as well as in providing sources of tissue for potential regenerative medicine therapies. An ideal bioengineered model of skeletal muscle should promote myoblast (muscle cell precursor) alignment as well as subsequent myoblast fusion into mature, multinucleated muscle cells known as myotubes. Accordingly, we report the development of an engineered protein biomaterial that promotes the alignment and fusion of primary human myoblasts into organized and differentiated myotubes. Furthermore, these aligned human myotubes exhibit markers of functional maturation including organization of sarcomeres (the force-generating apparatus within muscle) and induced contractility upon electrical stimulation. To achieve this goal, we utilize a protein-engineered biomaterial to investigate the roles of biomaterial surface topography and cell-adhesion ligand density in promoting human muscle cell fusion ex vivo. These two material properties are selected due to previous reports that they influence the morphology and differentiation of murine myogenic cells, including primary mouse myoblasts and the transformed C2C12 cell line [1–8]. Mouse-derived cells are used in the vast majority of in vitro muscle studies and have contributed greatly to our knowledge of muscle cell biology. However, few studies to date have used human muscle biopsies to isolate primary myoblasts[9–14], which are the most clinically relevant cell type, and a systematic analysis of biomaterial design criteria is lacking for human myoblasts. Here, we characterize the interactions of human primary myoblasts with a family of engineered biomaterials, and, for comparison, include the standard mouse-derived C2C12 cell line. While our results clearly demonstrate that human myoblasts, similar to C2C12 cells, are sensitive to surface topography and cell-adhesion ligand density, we also identify behavioral discrepancies indicating that C2C12 cells do not faithfully recapitulate the human myoblast response to biomaterial cues.

Scientific Abstract: